



# An olfactory subsystem that detects carbon disulfide and mediates food-related social learning

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## Abstract

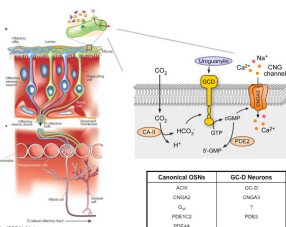
In mammals, pheromones and other social cues can promote mating or aggression behaviors; can communicate information about social hierarchies, genetic identity and health status; and can contribute to associative learning.

However, the molecular, cellular, and neural mechanisms underlying many olfactory-mediated social interactions remain poorly understood.

Here, we show a specialized olfactory subsystem that includes olfactory sensory neurons (OSNs) expressing the receptor guanylyl cyclase GC-D, the cyclic nucleotide-gated channel subunit CNGA3, and the carbonic anhydrase isoform CAII (GC-D(+) OSNs) is required for the acquisition of socially transmitted food preferences (STFPs) in mice.

## Introduction

Evidence for cAMP-independent olfactory responses



Frederick (2001) Nature

Figure 1. Approximately 1% of all olfactory receptors in mice are activated through a non-classical signal transduction cascade. These receptor neurons (GC-D(+) OSNs) work independently from the classical c-AMP signal transduction pathway. It has also been shown that these neurons are sensitive to CO<sub>2</sub> as a chemosensory stimulus

### Social Transmission of Food Preference (STFP)



Figure 2.

- Many mammals acquire food preferences from peers
- STFPs require the social odors from the breath of peers in addition to food odors
- STFP requires the coincidental detection of both a social odor (breath) and a food odor.
- The major components of breath are CO<sub>2</sub>, CS<sub>2</sub> and COS all of which are metabolized by carbonic anhydrase II (CAII).

## Experiment 1

### GC-D(+) OSNs are Highly Sensitive to Socialchemicals

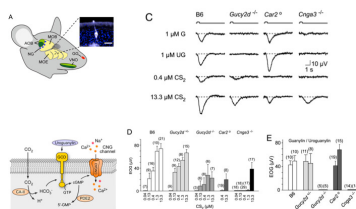


Figure 3. (A) OSNs in a genetically modified mice that lack different components of the olfactory signal transduction pathway can be visualized in situ using fluorescent imaging. (B) Signal transduction cascade in GC-D(+) OSNs. (C) Electroolfactograms (EOG) in genetically modified mice show deficit responses to semiochemicals. (D) Mean OEG responses in genetically modified mice to the sociochemical CS<sub>2</sub>. (E) Mean EOG responses to the socialchemicals Guanylin and Uroguanylin.

## Experiment 2

### Social Transmission of Food Preferences (STFP)

- Demonstrator mouse is fed food odored with a novel odor
- The Demonstrator is replaced into his colony and allowed to interact with "Observer" mice
- Observers are given a choice to eat food fed to the demonstrator or a novel food

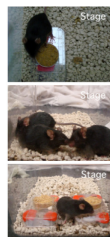


Figure 4. STFP Paradigm in which mice will communicate a preference for a particular food source

### Mice Lacking Functional GC-D(+) OSNs Fail to Acquire STFPs

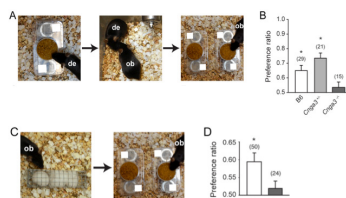


Figure 5. (A) STFP paradigm involving a live demonstrator mouse (B) Mice lacking a functional GC-D(+) OSN subsystem fail to prefer demonstrated food. (C) STFP paradigm involving a surrogate demonstrator tainted with food odor and the sociochemical CS<sub>2</sub>. (D) Mice lacking a functional GC-D(+) OSN subsystem fail to prefer food from surrogate demonstrator.

## Experiment 3

### A Functional GC-D(+) OSN System is required for the activation of Brain regions involved in STFP – associated learning

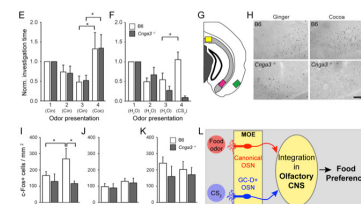


Figure 5. (E-F) Time mice spent investigating food and social odors (G-H) Representative photos of the c-Fos, a marker of neuronal activation (I-K) Mean c-Fos positive neurons in the hippocampus and entorhinal cortex of mice acquiring food preferences STFP paradigm involving a surrogate demonstrator tainted with food odor and the sociochemical CS<sub>2</sub>. (L) Model for the GC-D(+) OSN and classical OSNs interaction and associative learning

## Discussion

We conclude that GC-D(+) OSNs olfactory subsystem mediate the detection of social chemostimuli necessary for the formation of STFPs. Rodents and other animals make use of a diverse repertoire of chemical cues to communicate with conspecifics. While some of these chemostimuli may elicit innate behaviors, it is likely that most only have their full meaning in the context of additional sensory cues or previously learned associations. By linking a specific olfactory subsystem to both the expression of an established social learning behavior and to the detection of a chemostimulus that can elicit that behavior, we highlight the possibility that the subsystem structure of the mammalian main olfactory system may help mammals associate chemostimuli with other sensory cues in a meaningful and organized way.

## Conclusions

- A mammalian olfactory subsystem is essential for a type of social learning.
- A food-related social stimulus, CS<sub>2</sub>, activates specialized olfactory neurons.
- Mice with impaired CS<sub>2</sub> responses don't acquire socially transmitted food preferences.

## Acknowledgements

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